







CBD in public, professional sports and doping - regulatory issues, safety and effectiveness



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The CBD-hype

- CBD is big business: ~EUR 1.6 billion EU market 2020.
- Many recent scientific publications.
- Typical products: CBD-oils with 5-40% CBD.
- CBD is supposed to be good for... nearly everything!
- Consumers strongly believe in CBD.
- Placebo effects. Benefits yet to be scientifically proven.





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- A reduction of muscle damage and inflammatory processes after training is beneficial.
 - The prevalence of dietary supplements with antiinflammatory and antioxidant effects is increasing.
 - Interest in cannabidiol (CBD) products has been increasing, not only in recreational but also in competitive sports.
- There is only one approved CBD drug (Epidolex).













Cannabis and sports - an old story

Nagano, 1998. Snow Boarding gets olympic.

First winner is Ross Rebagliati, age 27.

Disqualification after a positive doping test – marihuana.

Got it back after protest. THC was not on the list of forbidden substances in 1998.







hooing im Ski und Snowboard-Spor parick Diel Enleitung mie in den meisten - und Snowboardniund Snowboarddisziplinen von der Geisel Dopings nicht verschont, Besonders der aufs und des Blathlons i aelte skandalträchtiger Naci ten Bei nivmpischen Wistennialen mi tößen, die selbst 2018 in Peronochano gal positive Oppingtests bei allerting 2019 in Seefeld. Hier wurden n auf frischer Tat ertappt und es Dopings, das mittle erden noch Jahre nach

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Since 1999 delta-9-Tetrahydrocannabinol (THC) is on the IOC list (later WADA) of forbidden substances.

- Cannabis increases the readiness to assume risk.
- Reduction of motoric abilities.
- Increased risk of fall.
- In summary an increased risk of injury.











- Cannabis and THC-cannabinoids • are forbidden in competition (day of competition)
- For positive detection there is set a ٠ limit of 150 ng/ml

But!

There is an exception for CBD



Anti-Doping regulations for Cannabis in 2023

Selegiline; Sibutramine Strychnine: Tenamfetamine (methylenedioxyamphetamine); Tuaminoheptane:

and other substances with a similar chemical structure or similar biological effect(s).

Except: Clonidine

· Imidazole derivatives for dermatological, nasal or ophthalmic use and those stimulants included in the 2020 Monitoring Program*.

- Bupropion, caffeine, nicotine, phenylephrine phenylpropanolamine, pipradrol, and synephrine: These substances are included in the 2020 Monitoring Program, and are not considered Prohibited Substances.
- Cathine: Prohibited when its concentration in urine is greater than 5 micrograms per milliliter. Ephedrine and methylephedrine: Prohibited when the concentration of either in urine is greater than 10 micrograms
- per milliliter. **** Epinephrine (adrenaline): Not prohibited in local administration, e.g. nasal, ophthalmologic, or co-administration with local anaesthetic agents
 - is greater than 150 micrograms per milliliter

GLUCOCORTICOIDS

All glucocorticoids are prohibited when administered by oral, intravenous, intramuscular or rectal routes

Including but not limited to:

Betamethasone Rudesonide-Cortisone: Deflazacort: Dexamethasone Fluticasone: Hydrocortisone Methylprednisolone;

Prednisolone Prednisone:

Triamcinolone.

NARCOTICS

The following narcotics, including all optical isomers, e.g. d- and l- where relevant, are prohibited: Buprenorphine;

Dextromoramide: Diamorphine [heroin]: Fentanyl and its derivatives Hydromorphone

Methadone;

Nicomorphine Oxycodone:

Oxymorphone Pentazocine Pethidine

CO CANNABINOIDS

All natural and synthetic cannabinoids are prohibited, e.g.

- · In cannabis (hashish, marijuana) and cannabis products
- Natural and synthetic tetrahydrocannabinols [THCs]
- Synthetic cannabinoids that mimic the effects of THC

Except:

Cannabidio



CANNABINOIDS

All natural and synthetic cannabinoids are prohibited, e.g.

- In cannabis (hashish, marijuana) and cannabis products
- Natural and synthetic tetrahydrocannabinols [THCs]
- Synthetic cannabinoids that mimic the effects of THC







Morphine;





Commentary

A Warning against the Negligent Use of Cannabidiol in Professional and Amateur Athletes

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MDPI

Abstract: Cannabidiol (CBD) is a non-psychoactive cannabinoid, widely marketed to athletes for claimed effects such as decreased anxiety, fear memory extinction, anti-inflammatory properties, relief of pain and for post-exercise recovery. The World Anti-Doping Agency (WADA) has excluded CBD from its list of prohibited substances. Nevertheless, caution is currently advised for athletes intending to use the compound—except CBD, all other cannabinoids are still on the prohibited list. CBD products, specifically non-medicinal, so-called full-spectrum cannabis extracts, may contain significant levels of these substances, but also contaminations of tetrahydrocannabinol (THC) (>2.5 mg/day in >30% of products on the German market) potentially leading to positive doping tests. Labelled claims about CBD content and absence of THC are often false and misleading. Contaminations with the psychoactive THC can result in adverse effects on cognition and, in general, the safety profile of CBD with respect to its toxicity is a controversial topic of discussion. For these reasons, we would currently advise against the use of over-the-counter CBD products, especially those from dubious internet sources without quality control.

Keywords: cannabis sativa; cannabidiol; delta-9-tetrahydrocannabinol; exercise nutritional science; doping in sports

Problem:

Many of the CBD products offered are not free of THC!

Clear recommendation for athletes:

To be safe and avoid testing positive, do not use CBD products !!





Cannabidiol (CBD) -Regulatory and Safety Aspects





In the EU CBD is considered to be a Novel Food

EU NF catalogue: Cannabis sativum L. extracts and derived products containing cannabinoids as well as synthetically obtained cannabinoids are considered NF in the EU as a history of consumption before 15 May 1997 has not been demonstrated.



Authorisation by European Commission required, based on a risk assessment by the European Food Safety Authority (EFSA). >150 CBD NF applications, 19 at EFSA, all incomplete.





EFSA Journal

Safety of CBD



ADOPTED: 26 April 2022 doi: 10.2903/j.efsa.2022.7322

Statement on safety of cannabidiol as a novel food: data gaps and uncertainties

EFSA Panel on Nutrition, Novel Foods and Food Allengers (NDA), Dominique Tuck, Tostas Boh, Jucqueine castennilles, Sefaan De Herauw, Karen Ilido Hitsch-Emst, Alexandre Maciuli, Inge Mangelsdof, Harry J McArde, Andronki Naska, Carmen Pelese, Kristina Petreka, Allenso Saint, Frank Sanghei Marthell, Monika Naukussee Derkold, Motern Turbusen, Mjuel Pritot Naradona Josef Rudratek, Monika Naukussee Derkold, Motern Turbusen, Mjuel Pritot Naradona Josef Cardina, Karaka Sanghei Cardina, Sanghei Sanghei Marthell, Marthe Maradona Esténan Nordea Ternandez, Amamana Rossa and Hele Kartine Krutsen

Abstract

The European Commission has determined that cannabidiol (CBD) can be considered as a novel food (NF), and currently, 19 applications are under assessment at EFSA. While assessing these, it has become clear that there are knowledge gaps that need to be addressed before a conclusion on the safety of CBD can be reached. Consequently, EFSA has issued this statement, summarising the state of knowledge on the safety of CBD consumption and highlighting areas where more data are needed Literature searches for both animal and human studies have been conducted to identify safety concerns. Many human studies have been carried out with Epidyolex[®], a CBD drug authorised to treat refractory epilepsies. In the context of medical conditions, adverse effects are tolerated if the benefit outweights the adverse effect. This is, however, not acceptable when considering CRD as a NE Furthermore, most of the human data referred to in the CBD applications investigated the efficacy of Epidyolex (or CBD) at therapeutic doses. No NOAEL could be identified from these studies. Given the complexity and importance of CBD receptors and pathways, interactions need to be taken into account when considering CBD as a NF. The effects on drug metabolism need to be clarified. Toxicokinetics in different matrices, the half-life and accumulation need to be examined. The effect of CBD on liver, pastrointestinal tract, endocrine system, nervous system and on psychological function needs to be clarified. Studies in animals show significant reproductive toxicity, and the extent to which this occurs in humans generally and in women of child-bearing age specifically needs to be assessed. Considering the significant uncertainties and data gaps, the Panel concludes that the safety of CBD as a NF cannot currently be established.

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Keywords: Cannabidiol, Novel Food, safety, data gaps

Requestor: European Commission Question number: EFSA-Q-2021-00735 Correspondence: nif@efsa.europa.eu

www.efsa.europa.eu/efsajournal

EFS/

EFSA (2022) «statement on safety of CBD as a Novel Food: "data gaps and uncertainties":

Safety can currently not be established.

Clock-stop, applicants to provide safety data.

Products still marketed are in violation of food legislation (unauthorized NF).



EFSA 2022 statement on safety of CBD as NF: data gaps and uncertainties



Epidyolex (or CBD) at therapeutic doses. No NOAEL could be identified from these studies. Given the complexity and importance of CBD receptors and pathways, interactions need to be taken into account when considering CBD as a NF. The effects on drug metabolism need to be clarified. Toxicokinetics in different matrices, the half-life and accumulation need to be examined. The effect of CBD on liver, gastrointestinal tract, endocrine system, nervous system and on psychological function needs to be clarified. Studies in animals show significant reproductive toxicity, and the extent to which this occurs in humans generally and in women of child-bearing age specifically needs to be assessed. Considering the significant uncertainties and data gaps, the Panel concludes that the safety of CBD as a NF cannot currently be established.



Clear evidence for liver toxicity. LOAEL healthy humans 4.3 mg CBD/kg bw/day. Studies in humans and animals needed.



Cannabidiol (CBD) -Mechanisms of action













Arachidonylethanolamide AEA The first identified endogenous CB-1 ligand (1992)



Differences between THC and CBD

Cannabidiolic acid (CBDA)

Cannabidiol (CBD)

Tetrahydrocannabinol (THC)







- Different affinities to CB1 and CB2
- THC has psychotropic activity via binding to CB1
- CBD does not show psychotropic activity







- Anabolic activity
- Antioxidative activity
- Anti-inflammatory activity
- Activation of stem cells
- Quality of sleep
- Psychological effects (relaxation)





Recovery in sports refers to the physiological and psychological processes that help an athlete restore their body and mind to pre-exercise states after intense physical activity.

These processes aid in:

- repairing tissue damage
- replenishing energy stores
- and reducing fatigue, ultimately facilitating enhanced performance and injury prevention.







The importance of recovery for training adaptation



Supercompensation







A variety of plant derived substances could be demonstrated to effect physical performance







An example: Ecdysterone



Fig.4 Results of strength tests performed pre- and post-intervention, 1-RM back squat (left), 1-RM bench press (right), * indicates time effect; # represents group \times time effect (both p < 0.05)

Archives of Toxicology https://doi.org/10.1007/s00204-019-02490-x

REGULATORY TOXICOLOGY



Ecdysteroids as non-conventional anabolic agent: performance enhancement by ecdysterone supplementation in humans

Eduard Isenmann^{1,2} · Gabriella Ambrosio² · Jan Felix Joseph^{3,4} · Monica Mazzarino⁵ · Xavier de la Torre⁵ · Philipp Zimmer^{1,6} · Rymantas Kazlauskas⁷ · Catrin Goebel⁷ · Francesco Botrè^{5,8} · Patrick Diel¹ · Maria Kristina Parr³¹

- Ecdysterone has proven anabolic activity.
- Is monitored by the WADA.
- Is developed as a drug.
- Whether uptake by food has any pharmacological effects is under investigation.





And does CBD effect physical performance?





Problem:

- There is a lack of evidence.
- Number of scientific studies is limited.
- Quality of these studies is poor.

The impact of CBD in sport - how CBD can help recovery and improve performance

Athletes often face intense physical stress, which can lead to injuries, pain and inflammation. In recent years, many athletes have harned to CBD to treat these aliments. In this article, we will discuss the effects of CBD in sport. How CBD poducts (such as CBD old; can help recovery and improve performance in sport. We also share the expediences of well-show athletes and how they have beerfiled from the use of CBD.

What is CBD?

CBD, or cannabidiol, is one of more than 100 cannabinoids found in hemp plants. Unlike THC (Tetrahydrocarnabinol), the psychoactive compound in connexis, CBD obses not cause introlocation or exphonia. Instead, CBD has many therapeutic effects, including pain relief, reducing inflammation, alleviating anxiety and improving steep quality

It is important to know the differences between the various CDD oils so that you can choose the right product for you. Full spectrum oils contain all the healthy cannabinoids, terpenes and flavonoids of the hemp plant. CDD lostels is a pure CDD compound with no other ingredients. Due to the lack of terpenes and flavonoids, the benefits of CBD isolate are more finited.



Benefits of CBD for athletes

We have written an extensive article on how CBD affects the human body. The same lessons apply to sport. For athletes, there are many benefits of using CBD, including:

1. Pain relief

Pain caused by intense physical exertion is a common problem for athletes. CBD has proven to be an effective pain reliever that works as well as many traditional painkliens, but without their side effects. For example, IAFL player Rob Conkinvals has acid he uses CDID to releve pain and speed up his recovery from linguist. In the ask is mentioned that CDID help his inside better, which is insortant for an athleter hercovery and performance.

2. Reducing inflammation

Inflammation is the body nature response to damage and intellion. However, excessive inflammation can lead to chronic park, pirit stiffless and their health proteins. 2010 has anti-inflammatory properties that can be produe inflammation and pseud health, MMA tight intellion, among others, has said that he has benefited from the anti-inflammatory effects of CBD bacause it has helped him recover faster from intense physical evention.

3. Anxiety relief

In competitive situations, atteies are often under a lot of pressure and stress, which often influents their performance. The cateling and anxietypics effects of CED helps in backet annihy and improve concentration, and in the base in motion to have performance in the lange limitative start is a carring sports competitions. Professional grade Fighter Fighter Four has all traits the use CED because in the band of improve this concentration and helps limit missi starting and the competition of the lange limit the lange limit the start is a lange limit to the lange limit the limit to the lange limit to the

4. Improving sleep quality

Good sleep quality is important for recovery and performance. CBD can help improve sleep quality and reduce insomnia, which can be particularly useful for athletes who travel frequently between time zones. For example, NBA player Kay Thiompson has reported using CBD to improve sleep quality and speed up recovery after games and practices.

5. Improving performance

Athough there is still title research on the direct effects of CBD on athletes' performance, many athletes have personally experienced the positive effects of CBD. The positive effects have also been nacload by footballer Megan Ripinco. He has reported using CBD to relieve pair, reduce inflammation and improve beep quality, which has helped him ingrove his position for field.



Literature CBD and performance

		Туре					
		of	Performanc				Period of
Autor	Year	paper	e tested	Titel	DOI	DOSE	application
Burr JF et al.	2021	Review	gerneral	Cannabis and Athletic Performance	<u>10.1007/s40279-021-01505-x</u>		
McCartney D et al.	2020	Review	general	Cannabidiol and Sports Performance: a Narrative Review of Relevant Evidence and Recommendations for Future Research	10.1186/s40798-020-00251-0.		
Kennedy MC	2022	Review	general	Cannabis: Exercise performance and sport. A systematic review.	10.1016/j.jsams.2017.03.012		
Isenmann E et al.	2020	RTC	power	Effects Of Cannabidiol Supplementation On The Skeletal Muscle - Regeneration After Intensive Resistance Training -Pilot Study	<u>10.1249/01.mss.0000683540.934</u> <u>33.31</u>	CBD 1.0 60mg	single
Isenmann E et al.	2021	RTC	power	Effects of Cannabidiol Supplementation on Skeletal Muscle Regeneration after Intensive Resistance Training	<u>10.3390/nu13093028</u>	CBD 2.0 60mg	single
Hatchett A et al.	2020	СТ	power	The Influence Cannabidiol on Delayed Onset of Muscle Soreness	10.1249/MSS.000000000002606	16mg	single
Cochrane-Snyman KC et al.	2021	RCT	power	The Effects of Cannabidiol Oil on Noninvasive Measures of Muscle Damage in Men	10.1249/MSS.000000000002606	150mg	2x75mg 3 days
Crossland BW et al.	2022		power	Acute Supplementation with Cannabidiol Does Not Attenuate Inflammation or Improve Measures of Performance Following Strenuous Exercise	10.3390/healthcare10061133	224-408mg	single 5mg/kg
Lisano JK et al.	2022	Cross- sectional Study	endurance	Regular Use of Cannabis in Female Athletes Is Associated With a Reduction in Farly Anaerobic Power Production	10.1519/ISC.000000000004297	no data	
Sahinovic A et al.	2022	RCT	endurance	Effects of Cannabidiol on Exercise Physiology and Bioenergetics: A Randomised Controlled Pilot Trial.	10.1186/s40798-022-00417-y	300mg	single
Isenmann E et al.	2023	RCT	Power/endurance	Influence of short-term chronic cannabidiol application on muscle damage and performance after an intensive training week - a randomised double-blind crossover study	unpublished	60mg	7 Days 60mg





Background: The consumption of cannabidiol (CBD) to support recovery and enhance performance has become popular among athletes.

Scientific Rational: Potential anti-inflammatory and anti-oxidative properties of CBD are supposed to result in pro-regenerative effects after strength training.

Scientific Question: Therefore, we have conducted three intervention studies to investigate the effects of CBD treatment on performance and muscle recovery after resistance training.









Study No. 1. Pilot Study - Investigation of proregenerative effects of a single CBD supplementation after intensive resistance training

Study design: Randomised, double blinded crossover- design

10 resistance training experienced young man Intensive resistance training

Application of 3ml CBD solution (60mg, >99% CBD) or placebo

4 weeks wash out between interventions









Study No. 1. Pilot Study - Investigation of proregenerative effects of a single CBD application after intensive resistance training

Results: power 24h after training

CK in serum 24h after training



24h after training in the CBD group power is reduced but also CK as a marker for skeletal muscle damage.



Study No. 2. Investigation of time dependent proregenerative effects of a single CBD application after intensive resistance training



Study design. BS = Back Squat; reps = Repetitions; s = second; 1RM; One-Repetition Maximum; h = hours.





Study No. 2. Investigation of time dependent proregenerative effects of a single CBD application after intensive resistance training



Markers for skeletal muscle damage are reduced in the CBD group.

Strength after 72 training is higher in the CBD group.

Astox Wien 30.11.2023

T72



Agency (CVUA) Karlsruhe).

Study No. 3. Investigation the effects of a cornical CBD supplementation during an intensive training week





Study No. 3. Results Power



Counter movement jump



Back squat





Study No. 3. Muscle Damage

Creatine Kinase

Myoglobin





Markers for liver toxicity





Study	Study design	Perfomance level	Training protocol	Treatment	Number of application	Measuring points	Paramters
A	6 arm cross-over RCT washout period: 2 weeks	well-trained (n=16)	3sets 12 reps BS@70% of 1RM 3 sets of 15 reps Drop Jumps	1.) CBD solubilisat (60mg) 2.) Placebo	single application after training (following 3h after training no further applications were allowed)	T0 (pre) T24h T48h T72h	performance: 1RM BS; CMJ muscle damage: CK; Myo
В	2 arm cross-over RCT washout period: 3 weeks	highly well- trained (n=8)	3sets 12 reps BS@70% of 1RM 3 sets of 15 reps Drop Jumps	1.) CBD solubilisat (60mg) 2.) Placebo	single application after training (following 3h after training no further applications were allowed)	T0 (pre) T24h	performance: 1RM BS; CMJ muscle damage: CK
с	3 arm cross-over RCT washout period: 3 weeks	well-trained (n=8) highly well- trained (n=8)	training 3x strength training 3x high intensity intervall training	1.) CBD solubilisat (60mg) 2.) CBD oil (60mg) 3.) Placebo	short-term chronic application; each day after training beginning after pre-test	T0 (pre) T168h (one week)	performance: 1RM BS; 1RM BP; CMJ; 1mile run muscle damage: CK; Myo

Conclusion of own investigations

- The results indicate small but significant effects of a single CBD application after strength training on muscle damage.
- Effects varied depending on the performance level.
- First trends suggest similar effects after short-term repeated treatment.
- On performance, the results are currently inconsistent. Therefore, further human studies are needed.
- A doses 60 mg CBD a day does not result in increase of markers for liver toxicity.
- Training induced increase of GPT could be antagonized by CBD application.



Flores, V.A.; Kisiolek, J.N.; Ramani, A.; Townsend, R.; Rodriguez, E.; Butler, B.; Stewart, L.K. Effects of Oral Cannabidiol on Health and Fitness in Healthy Adults: An 8-Week Randomized Trial. *Nutrients* **2023**, *15*, 2664.



Conclusions The present study observed that daily consumption of 50 mg of CBD for 8 weeks did not result in significant improvements in body composition, aerobic and other muscular strength measures, mental health, or inflammation in physically active adults. However, CBD supplementation appeared to attenuate decreases in peak anaerobic power over time. The study also observed a possible effect of CBD on average power output, which warrants further investigation. The limitations of the present study should also be considered when interpreting the results. Future studies should consider longer intervention durations, higher CBD doses, and monitoring physical activity and exercise training during the intervention period. Overall, these findings contribute to the limited knowledge surrounding the effects of CBD on physical fitness, mental health, and inflammation, and highlight the need for further research to fully understand the potential benefits and limitations of CBD consumption in healthy individuals.





Overall conclusion

- Based on published data but also on own investigations there is currently no clear evidence for performance enhancing effects of CBD supplementation.
- Effects depend on a variety of individual factors like training status, training mode and more.
- Other plant derived substances tested in a similar setting show stronger effects.
- Liver toxicity of CBD after chronical application for longer periods is still unclear.
- Orally consumption of CBD products in the EU is currently illegal.
- Contamination of CBD products by THC can result in positive doping tests.

Therefore currently risk/benefit ratio counts against use of CBD products to enhance performance.







Thanks to :

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